JAN 13 2011

SECTION 2

510(k) SUMMARY

510(k) SUMMARY:
This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: _____

DATE: November 20th, 2009

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PRODUCT TRADE NAME: Bio-Rad Laboratories Platelia™ *Aspergillus* EIA

COMMON NAME: *Aspergillus* Antigen EIA

CLASSIFICATION NAME: Antigen, Galactomannan, *Aspergillus* spp.

PREDICATE DEVICE: Platelia™ *Aspergillus* EIA

DEVICE DESCRIPTION

The Platelia™ *Aspergillus* EIA is a one-stage immunoenzymatic sandwich microplate assay which detects galactomannan in human serum and BAL fluid samples. The assay uses rat EBA-2 monoclonal antibodies, which are directed against *Aspergillus* galactomannan, and have been characterized in previous studies. The monoclonal antibodies are used, (1) to coat the wells of the microplate and bind the antigen, and (2) to detect the antigen bound to the sensitized microplate (conjugate reagent: peroxidase-linked monoclonal antibodies).

Serum or BAL fluid samples are heat-treated in the presence of EDTA in order to dissociate immune complexes and to precipitate proteins that could possibly interfere with the test. The treated samples and conjugate are added to the wells coated with monoclonal antibodies, and incubated. A monoclonal antibody – galactomannan - monoclonal antibody / peroxidase complex is formed in the presence of galactomannan antigen.

The strips are washed to remove any unbound material. Next, the substrate solution is added, which will react with the complexes bound to the well to form a blue color reaction. The enzyme reaction is stopped by the addition of acid, which changes the blue color to yellow. The absorbance (optical density) of specimens and controls is determined with a spectrophotometer set at 450 and 620/630 nm wavelength.

INTENDED USE

The Platelia™ *Aspergillus* EIA is an immunoenzymatic sandwich microplate assay for the detection of *Aspergillus* galactomannan antigen in adult and pediatric serum and Bronchoalveolar Lavage (BAL) fluid samples.

The Platelia™ *Aspergillus* EIA is a test which, when used in conjunction with other diagnostic procedures such as microbiological culture, histological examination of biopsy samples and radiographic evidence, can be used as an aid in the diagnosis of Invasive Aspergillosis.

INDICATIONS FOR USE

The Platelia™ *Aspergillus* EIA is an immunoenzymatic sandwich microplate assay for the detection of *Aspergillus* galactomannan antigen in adult and pediatric serum and Bronchoalveolar Lavage (BAL) fluid samples.

The Platelia™ *Aspergillus* EIA is a test which, when used in conjunction with other diagnostic procedures such as microbiological culture, histological examination of biopsy samples and radiographic evidence, can be used as an aid in the diagnosis of Invasive Aspergillosis.

TECHNOLOGICAL CHARACTERISTICS

The following tables summarize similarities and differences between the Platelia™ *Aspergillus* EIA (62793) and the current Platelia™ *Aspergillus* EIA (k060641):

Table 1(a) Similarities between intended use

Similarities in Function and Use	**Platelia™ *Aspergillus* EIA, Catalog 62793**	**Platelia™ *Aspergillus* EIA current (k060641)**
Intended Use	Galactomannan antigen detection.	Galactomannan antigen detection.

Table 1(b) Differences between intended use

Differences in Function and Use	**Platelia™ *Aspergillus* EIA, Catalog 62793**	**Platelia™ *Aspergillus* EIA (k060641)**
Intended Use	Detection of *Aspergillus* galactomannan antigen in adult and pediatric serum and Bronchoalveolar Lavage (BAL) Fluid samples.	Detection of *Aspergillus* galactomannan antigen in adult and pediatric serum samples.
Matrix	Serum and Bronchoalveolar Lavage (BAL) Fluid samples	Serum
Intended Use /Indications for Use	Both the Intended Use and Indications for Use are same.	The Intended Use and Indications for Use are different.

Table 2 Similarities between reagents and materials

Similarities in Components / Materials	**Platelia™ *Aspergillus* EIA, Catalog 62793**	**Platelia™ *Aspergillus* EIA (k060641)**
Microplate	96 well microplate – antibody coated microwells	96 well microplate – antibody coated microwells
Reagents	Conjugate, Wash Buffer, Substrate, TMB Chromogen, Sample Diluent, Positive Control, Stop Solution.	Conjugate, Wash Buffer, Substrate, TMB Chromogen, Sample Diluent, Positive Control, Stop Solution.

Table 3 Similarities between assay procedures.

Similarities in Assay Procedures	**Platelia™ *Aspergillus* EIA, Catalog 62793**	**Platelia™ *Aspergillus* EIA (k060641)**
Incubation temperature of the microplate after addition of the conjugate and the treated sera.	Incubation temperature: 37°C	Incubation temperature: 37°C
Incubation time of the microplate after addition of the conjugate and the treated sera.	Incubation time: 90 ± 5 minutes	Incubation time: 90 ± 5 minutes

Table 4 Differences between Limitations of the Procedure

Differences in Limitations of the Procedure (Section 13)	**Platelia™ *Aspergillus* EIA, Catalog 62793**	**Platelia™ *Aspergillus* EIA (k060641)**
Limitation: Point 11	Addition of Histoplasma and Geotrichum to the list of fungi causing cross-reactivity	
Limitation: Point 12	Addition of a limitation that cross-reactivity of BAL fluid with Mycoplasma and anaesthetic drugs used to numb the neck/throat area has not been evaluated.	
Limitation: Point 13	Addition of limitation regarding positive reactions observed in patients receiving products containing sodium gluconate, galactofuranose or galactomannan.	
Limitation: Point 14	Addition of limitation regarding positive reactions observed in patients receiving PLASMA-LYTE™ solution.	
Limitation: Point 15	Addition of limitation about assay results in BAL fluid samples from immunocompromised patients to be interpreted with caution.	

Limitation: Point 16	Results of the Platelia™ *Aspergillus* EIA in Bronchoalveolar Lavage (BAL) fluid samples between 0.5-1.0 index have a lower predictive value than BAL sample results > 1.0 index values, therefore the results between 0.5-1.0 index values should be reviewed and supported by other clinical, radiological or laboratory evidence of invasive aspergillosis[8, 17]	

PERFORMANCE EVALUATION SUMMARY

A. EXPECTED VALUES

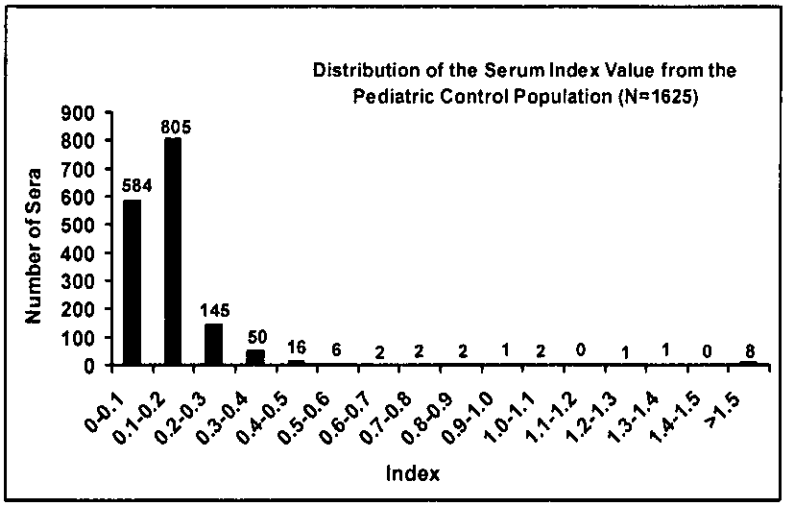
I. SERUM

The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported.
The following results have been obtained from clinical studies conducted on pediatric (age ≤ 21 years) patients in the United States and on adult patients in North America.

A.-Pediatrics
A clinical study was conducted on a total of 1954 serum samples from 129 immunocompromised pediatric (Age ≤ 21 years) patients, at high risk for Invasive Aspergillosis (IA) and patients diagnosed with Proven and Probable Invasive Aspergillosis, at three testing centers in the United States to determine the performance characteristics of the Platelia™ *Aspergillus* EIA. The distribution of index values for these populations is shown in the following charts:

Pediatric Patients diagnosed without Invasive Aspergillosis (control population)
A total of 1625* pediatric serum samples obtained from 108 immunocompromised pediatric patients at three testing centers in the United States were tested to determine the performance characteristics of the Platelia™ *Aspergillus* EIA. The distribution of index values for samples is shown in the following chart:

Figure 1

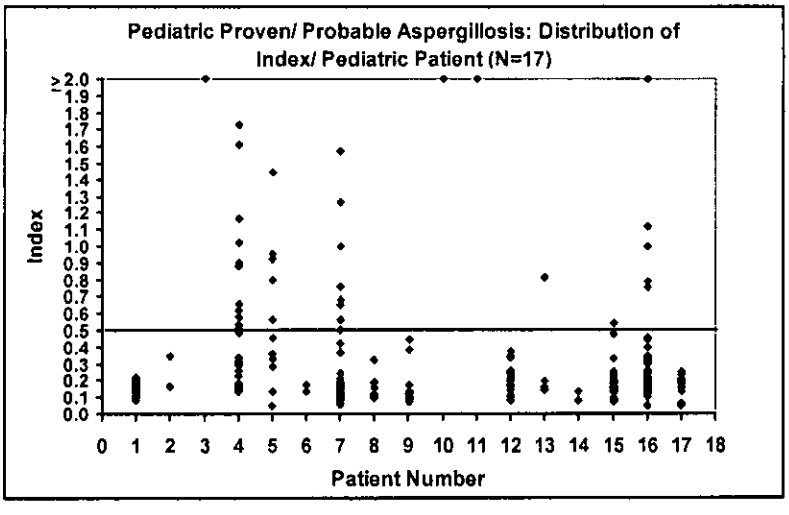


*Note: 80 samples, from 4 control patients with positive galactomannan antigen results coinciding with piperacillin/tazobactam (Zosyn®) therapy were excluded.

Pediatric Patients diagnosed with Invasive Aspergillosis

The scatter plot depicts galactomannan assay results for the 249 serum samples from 17 patients in this study diagnosed with proven or probable Invasive Aspergillosis as defined by EORTC/NIAID definitions. Not every serum sample from each patient is expected to be positive. The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported[10, 23]. The prevalence rate of this study was 13.6%.

Figure 2

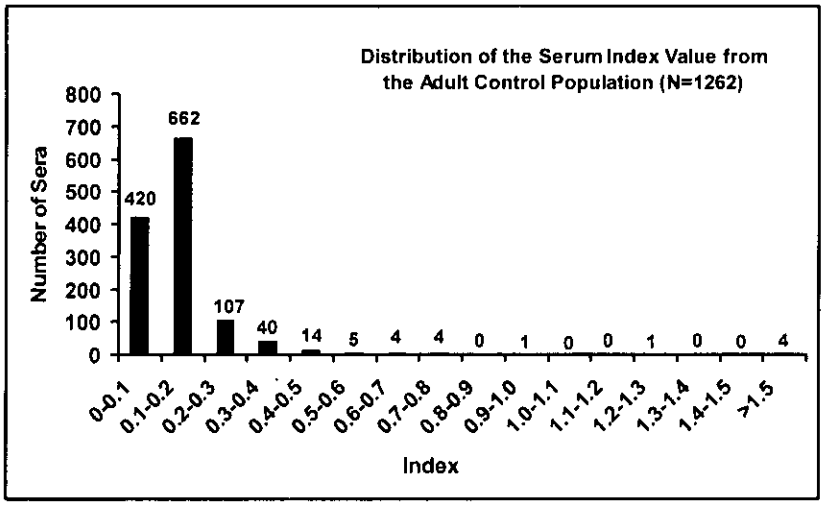


B. Adults

A clinical study was conducted on a total of 1724 serum samples from 172 bone marrow transplant (BMT) and leukemic patients diagnosed with and without Invasive Aspergillosis, at three testing centers in North America to determine the performance characteristics of the Platelia™ *Aspergillus* EIA. The distribution of index values for these populations is represented in the following charts.

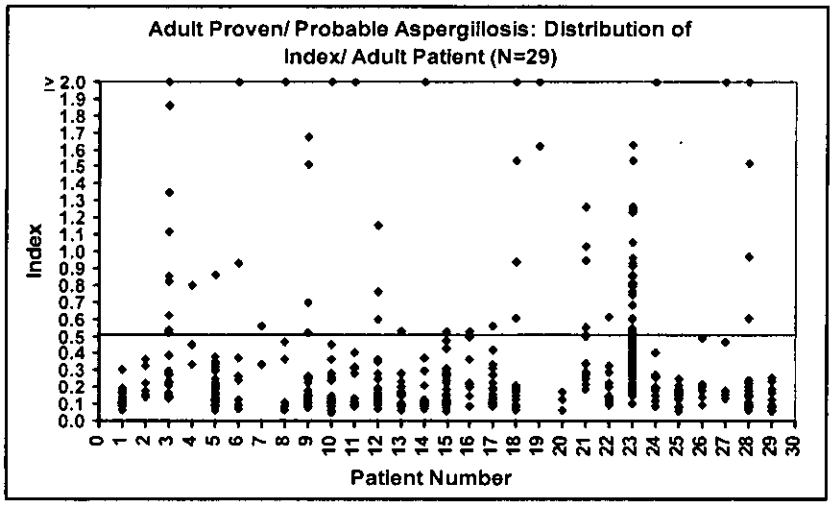
Adult Patients diagnosed without Invasive Aspergillosis (control population)
A total of 1262 serum samples obtained from 143 bone marrow transplant (BMT) and leukemic patients at three testing centers in North America were tested with the Platelia™ *Aspergillus* EIA test. The distribution of index values is shown in the following chart:

Figure 3



Adult Patients diagnosed with Invasive Aspergillosis
This scatter plot depicts galactomannan assay results for the 462 serum samples from 29 patients in this study diagnosed with proven or probable Invasive Aspergillosis as defined by EORTC/NIAID definitions. Not every serum sample from each patient is expected to be positive. The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported [10, 23]. The prevalence rate for this study was 16.9%.

Figure 4



The following graphs represent examples of a patient without clinical signs or symptoms of Invasive Aspergillosis (negative for *Aspergillus*) and a patient with proven or probable Invasive Aspergillosis (positive for *Aspergillus*) respectively.

Figure 5
Negative patient

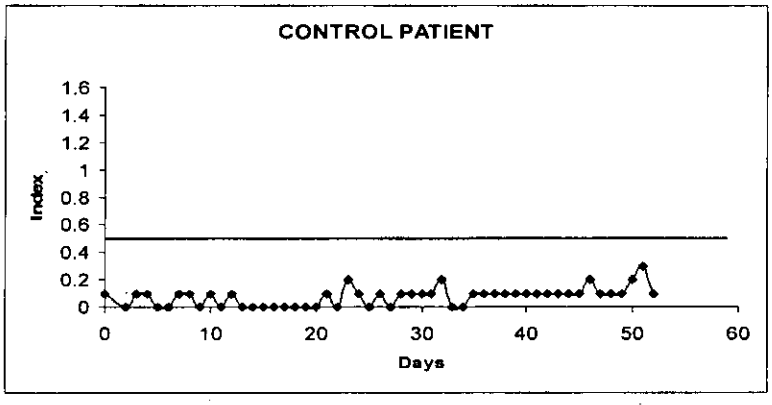
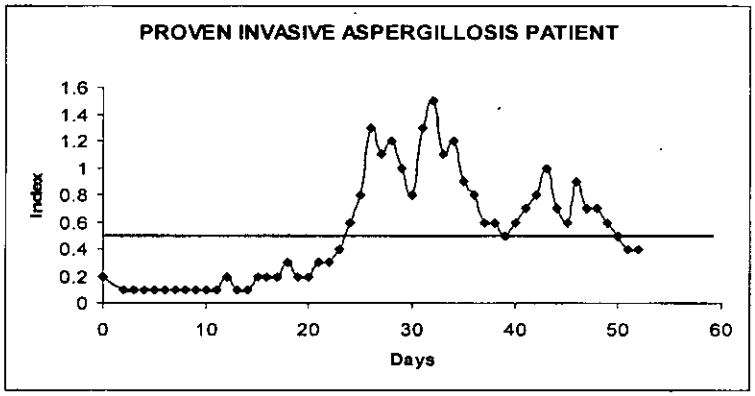


Figure 6
Positive patient



II. BAL FLUID

Two studies were conducted on a total of 449 BAL samples from 178 Solid Organ transplant (SOT) and lung transplant recipients with and without invasive aspergillosis in the United States to determine the performance characteristics of the Platelia™ *Aspergillus* EIA kit with Bronchoalveolar Lavage Fluid samples.
Of these, there were 403 BAL samples from 167 solid organ and lung transplant recipients without invasive aspergillosis.
In addition, a retrospective analysis was performed on BAL samples from 99 evaluable high risk haematology patients in a study outside the United States which included 58 patients with proven or probable invasive aspergillosis.

Expected values in BAL samples from the combined SOT and lung transplant recipients without Invasive Aspergillosis are presented in the table below. Results are presented by samples from transplant recipients with and without mold colonization.

Table 1

Expected Values by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis
N =403 BAL Fluids

Diagnosis	N	Positive (%)	Negative (%)
Controls without colonization	341	11/341(3.2%)	330/341(96.8%)
Controls with colonization	62	12/62 (19.4%)	50/62 (80.6%)
Control **Total**	403	23/403(5.7%)	380/403(94.3%)

Expected values in BAL samples from the combined SOT and lung transplant recipients without Invasive Aspergillosis are presented by transplant type in the table below.

Table 2

Expected Values by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis
By Transplant Type
N =403 BAL Fluids

Transplant Type	N	Positive (%)	Negative (%)
Heart	28	3/28 (10.7%)	25/28 (89.3%)
Kidney	25	3/25 (12.0%)	22/25 (88.0%)
Liver	23	1/23 (4.3%)	22/23 (95.7%)
Lung	327	16/327 (4.9%)	311/327 (95.1%)
Control **Total**	403	23/403 (5.7%)	380/403 (94.3%)

Expected values were also evaluated in a total of 41 BAL fluid samples from 41 hematological disease patients without Invasive Aspergillosis and are presented in the Table below

Table 3

Expected Values by Sample
Hematologic disease patients without Invasive Aspergillosis
N =41 BAL Fluids

Diagnosis	N	Positive (%)	Negative (%)
Controls	41	8/41 (19.5%)	33/41 (80.5%)

B. REPRODUCIBILITY STUDIES

a) Reproducibility Studies In Serum

Inter-assay and Intra-assay variability for the Platelia™ *Aspergillus* EIA were determined in a study using a panel of 6 pooled patient serum samples (one negative, one low positive, two positive, and two high positive) obtained at three clinical trial sites in North America. Each of the 6 panel members were tested in triplicate (x3) on 3 different days, on one lot, at two sites (total number of replicates at each site = 9). Each of the 6 panel members was tested in duplicate (x2) on 3 different days, on 1 lot, at a third site (total number of replicates at the third site = 6). One (1) operator performed all precision testing at each site. The data were analyzed according to the Clinical Laboratory Standards Institute (CLSI) (formerly National Committee for Clinical Laboratory Standards (NCCLS)). The mean optical density (OD) and mean index value, standard deviation (SD), percent coefficient of variation (%CV), within run precision (intraassay) and within site (inter-assay) precision for each panel member at each site are illustrated below in the following tables.

Table 4

Site 1

Panel Member	Neg		Low Pos		Pos #1		Pos #2		High Pos#1		High Pos #2		Neg Control		CO Control		Pos Control	
	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
N	9	9	9	9	9	9	9	9	9	9	9	9	3	3	6	6	3	3
Mean	0.052	0.09	0.445	0.74	0.702	1.17	0.931	1.563	1.227	2.06	2.887	4.83	0.046	0.08	0.606	1.00	2.216	3.67
Within Run (intra-assay)[1] SD	0.002	0.00	0.022	0.03	0.059	0.09	0.044	0.08	0.051	0.09	0.089	0.17	N/A	N/A	0.02	0.03	N/A	N/A
%CV	N/A	N/A	4.8%	4.4%	8.4%	7.6%	4.7%	5.1%	4.2%	4.4%	3.1%	3.6%	N/A	N/A	3.7%	3.4%	N/A	N/A
Total (inter-assay)[2] SD	0.036	0.04	0.051	0.08	0.070	0.14	0.044	0.25	0.058	0.29	0.169	0.58	N/A	N/A	0.102	0.03	0.317	0.12
%CV	N/A	N/A	11.5%	10.4%	10.0%	11.6%	4.7%	15.7%	4.7%	14.3%	5.9%	11.9%	N/A	N/A	16.9%	2.8%	14.3%	3.3%

Site 2

Panel Member	Neg		Low Pos		Pos #1		Pos #2		High Pos#1		High Pos #2		Neg Control		CO Control		Pos Control	
	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
N	9	9	9	9	9	9	9	9	9	9	9	9	3	3	6	6	3	3
Mean	0.040	0.10	0.280	0.70	0.364	0.89	0.602	1.49	0.801	2.01	1.381	3.43	0.074	0.18	0.415	1.00	1.197	2.97
Within Run (intra-assay)[1] SD	0.006	0.01	0.041	0.09	0.023	0.07	0.045	0.11	0.046	0.10	0.047	0.11	N/A	N/A	0.00	0.01	N/A	N/A
%CV	N/A	N/A	14.5%	13.0%	6.4%	7.6%	7.5%	7.1%	5.7%	4.8%	3.5%	3.2%	N/A	N/A	1.1%	1.1%	N/A	N/A
Total (inter-assay)[2] SD	0.006	0.03	0.058	0.19	0.083	0.18	0.057	0.28	0.042	0.53	0.079	1.00	N/A	N/A	0.094	0.01	0.068	0.54
%CV	N/A	N/A	20.8%	27.0%	22.7%	19.8%	9.5%	18.7%	5.3%	26.5%	5.8%	29.2%	N/A	N/A	22.7%	0.9%	5.7%	18.2%

Site 3

Panel Member	Neg		Low Pos		Pos #1		Pos #2		High Pos#1		High Pos #2		Neg Control		CO Control		Pos Control	
	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
N	6	6	6	6	6	6	6	6	6	6	6	6	3	3	6	6	3	3
Mean	0.049	0.10	0.388	0.81	0.652	1.36	0.830	1.73	1.158	2.41	2.378	4.96	0.059	0.12	0.480	1.00	1.652	3.45
Within Run (intra-assay)[1] SD	0.003	0.01	0.009	0.02	0.082	0.17	0.068	0.14	0.094	0.20	0.126	0.25	N/A	N/A	0.028	0.06	N/A	N/A
%CV	N/A	N/A	2.4%	2.4%	12.5%	12.2%	8.2%	8.2%	8.1%	8.2%	5.3%	5.1%	N/A	N/A	5.8%	5.8%	N/A	N/A
Total (inter-assay)[2] SD	0.012	0.03	0.078	0.13	0.068	0.15	0.104	0.25	0.082	0.15	0.111	0.34	N/A	N/A	0.028	0.04	0.056	0.23
%CV	N/A	N/A	20.0%	15.8%	10.5%	11.1%	12.5%	14.3%	7.1%	6.2%	4.7%	6.8%	N/A	N/A	5.8%	4.1%	3.4%	6.8%

N/A = not applicable

[1]NCCLS EP5-A, Vol. 19, No. 2, Page 24, Equation (C2)

[2]NCCLS EP5-A, Vol. 19, No. 2, Page 25, Equation (C3) and Equation (C4)

b) Reproducibillity Studies in BAL

Inter-assay and Intra-assay variability for the Platelia™ *Aspergillus* EIA were determined in a study using a panel of 4 pooled patient BAL samples spiked with purified galactomannan (one negative, one high negative, one low positive and one medium positive) at 3 testing sites (Two US clinical testing sites and one internal site). Each of the 4 panel members and the controls were tested in duplicate (x2) in 2 runs per day on 5 different days on one lot (Total number of replicates at each site = 120). Two (2) operators performed all precision testing at each site. The data was analyzed according to the Clinical Laboratory Standards Institute (CLSI) (formerly National Committee for Clinical Laboratory Standards (NCCLS)). The mean optical density (OD) and mean index value, standard deviation (SD), percent coefficient of variation (%CV), within run precision (intra-assay) and between site, between day, between operator and between run (inter-assay) precision for each panel member are illustrated below in the following table:

Table 5

Combined Sites Summary

Summary		Negative N= 60		High Negative N=60		Low Positive N=60		Medium Positive N=60		Positive Control N=60		Negative Control N=60	
		OD	Index	OD	Index	OD	Index	OD	Index	OD	Index	OD	Index
Mean		0.121	0.29	0.214	0.50	0.375	0.88	0.575	1.35	1.580	3.72	0.047	0.11
Within Run (Intra Assay)	**SD**	N/A	N/A	0.037	0.103	0.035	0.078%	0.029	0.067	0.111	0.265	N/A	N/A
	%CV	N/A	N/A	17.4%	20.5%	9.3%	8.9%	5.0%	5.0%	7.0%	7.1%	N/A	N/A
Total (Inter Assay)	**SD**	N/A	N/A	0.042	0.095	0.061	0.122	0.070	0.138	0.190	0.438	N/A	N/A
	%CV	N /A	N/A	19.6%	18.9%	16.2%	13.9%	12.2%	10.2 %	12.0%	11.8 %	N/A	N/A

C. PERFORMANCE EVALUATION STUDIES

I. SERUM SAMPLES

Clinical testing to evaluate the sensitivity, specificity, and predictive value of the Platelia™ *Aspergillus* EIA was conducted on pediatric (age ≤ 21 years) patients at three sites located in the United States and on adult patients at three sites located in North America. The studies were conducted using a total of 1954 serum samples collected from 129 pediatric patients and a total of 1724 serum samples collected from 172 adult patients from the following populations*:

- patients without signs of Invasive Aspergillosis (control patients)
- patients with Probable Invasive Aspergillosis
- patients with Proven Invasive Aspergillosis

* The Invasive Fungal Infection Cooperative Group (IFICG) of the European Organization for Research and Treatment of Cancer (EORTC) and the Mycosis Study Group (MSG) of the National Institute of Allergy and Infectious Diseases (NIAID) in 2002 have defined criteria for diagnosis of Invasive Aspergillosis (IA) in patients with hematologic malignancy or hematopoetic stem cell transplant.[2]

SENSITIVITY

A. Pediatrics

Results from this study have been analyzed in terms of patient sensitivity. Sensitivity testing was conducted using the Platelia™ *Aspergillus* EIA at three sites on a combined total of 17 immunocompromised pediatric patients diagnosed with Proven or Probable Invasive Aspergillosis.

Table 6

Diagnosis	Number of patients	Sensitivity	95% Confidence Interval
Proven Aspergillosis	9	44.4% (4/9)	18.9-73.3%
Probable Aspergillosis	8	62.5% (5/8)	30.6-86.3%
Combined Proven and Probable Aspergillosis	17*	52.9% (9/17)	31.0-73.8%

*Note: 8 of the 17 patients gave negative *Aspergillus* galactomannan antigen results. All of the 8 patients with negative *Aspergillus* galactomannan antigen results received therapy with multiple antifungal agents. The concomitant use of mold-active anti-fungal therapy in some patients with Invasive Aspergillosis may result in reduced sensitivity[31].

B. Adults

Sensitivity testing was conducted using the Platelia™ *Aspergillus* EIA at three sites on a combined total of 29 Bone Marrow Transplant (BMT) and Leukemia adult patients diagnosed with Proven or Probable Invasive Aspergillosis.

Table 7

Diagnosis	Number of patients	Sensitivity	95% Confidence Interval
Proven Aspergillosis	11	81.8% (9/11)	52.3-94.9%
Probable Aspergillosis	18	77.8% (14/18)	54.8-91.0%
Combined Proven and Probable Aspergillosis	29	79.3% (23/29)	61.6-90.2%

SPECIFICITY

A. Pediatrics

Specificity by pediatric patients

Specificity testing was conducted using the Platelia™ *Aspergilllus* EIA at three sites on a combined total of 108* immunocrompomised pediatric patients without signs of Invasive Aspergillosis (control patients).

Table 8

Site	Number of patients	Specificity	95% Confidence Interval
1	44	86.4 % (38/44)	73.3-93.6%
2	59	86.4 % (51/59)	75.5-93.0%
3	5	100% (5/5)	56.6-100%
Combined Sites	108	87.0% (94/108)	79.4-92.1%

*Note: 4 patients with positive galactomannan antigen results coinciding with piperacillin / tazobactam therapy were excluded.

Specificity by pediatric samples

Specificity testing was conducted using the Platelia™ *Aspergilllus* EIA at three sites on a combined total of 1625* samples obtained from 108 immunocrompomised pediatric patients without signs of Invasive Aspergillosis (control patients).

Table 9

Site	Number of samples	Specificity	95% Confidence Interval
1	794	98.9% (785/794)	97.9-99.4%
2	731	97.8% (715/731)	96.5-98.6%
3	100	100% (100/100)	96.3-100%
Combined Sites	1625	98.5% (1600/1625)	97.7-99.0%

*Note: 80 samples from 4 patients with positive galactomannan antigen results coinciding with piperacillin / tazobactam therapy were excluded.

B. Adults

Specificity by adult patients

Specificity testing was conducted using the Platelia™ *Aspergillus* EIA at three sites on a combined total of 143 Bone Marrow Transplant (BMT) and Leukemia adult patients without signs of Invasive Aspergillosis (control patients).

Table 10

Site	Number of patients	Specificity	95% Confidence Interval
1	28	78.6% (22/28)	60.5-89.8%
2	77	93.4% (71/77)	84.0-96.4%
3	38	89.5% (34/38)	75.9-95.8%
Combined Sites	143	88.8% (127/143)	82.6-93.0%

Specificity by adult samples

Specificity testing was conducted using the Platelia™ *Aspergillus* EIA at three sites on a combined total of 1262 samples obtained from 143 Bone Marrow Transplant (BMT) and Leukemia adult patients without signs of Invasive Aspergillosis (control patients).

Table 11

Site	Number of samples	Specificity	95% Confidence Interval
1	349	98.0% (342/349)	95.9-99.0%
2	560	98.6% (552/560)	97.2-99.3%
3	353	98.9% (349/353)	97.1-99.6%
Combined Sites	1262	98.5% (1243/1262)	97.7-99.0%

PREDICTIVE VALUE

Positive and negative predictive values have been analyzed for the patient population in this study. Based on the actual average of 13.6% prevalence rate in pediatrics and 16.9% prevalence rate in adults observed in this study, positive and negative predictive values have been calculated as below:

A. Pediatrics

Study Prevalence 13.6%

PPV: 39.1% 95% Confidence Interval : 22.2-59.2%
NPV: 92.2% 95% Confidence Interval : 85.3-96.0%

B. Adults

Study Prevalence 16.9%

PPV: 59.0% 95% Confidence Interval:43.4-72.9%
NPV: 95.5% 95% Confidence Interval: 90.5-97.9%

The expected prevalence of Invasive Aspergillosis varies with the patient population; rates from 5-20% have been reported[10, 23]. For patient populations on the lower end of the

published prevalence, the positive and negative predictive values have been re-calculated using a 5% prevalence rate.

A. Pediatrics

Calculated Prevalence 5%

PPV : 17.6% 95% Confidence Interval : 6.5-39.8%
NPV : 97.2% 95% Confidence Interval : 92.1-99.1%

B. Adults

Calculated Prevalence 5%

PPV: 27.2% 95% Confidence interval: 13.7-46.7%
NPV: 98.8% 95% Confidence Interval: 95.4-99.7%

CROSS REACTIVITY

a) Cross Reactivity - Serum

A study to evaluate the effect of potentially interfering medical conditions unrelated to Invasive Aspergillosis was performed with one lot of the Platelia™ *Aspergillus* EIA kit. The following serum samples were tested for cross-reactivity with the Platelia™ *Aspergillus* EIA. A total of 151 sera were tested.

Table 12

Pathology	# Samples Tested	# Positives
Rheumatoid Factor	10	0
ANA Positive	10	0
IgG Hypergammaglobulinemia	10	0
IgM Hypergammaglobulinemia	10	0
Cancer*	11	0
Non-Viral Cirrhosis (primary biliary; alcohol induced; drug induced)	10	0
Multiple Transfusions	10	0
Multiparous Females	10	0
HAV	10	0
HCV	10	0
Rubella	10	0
CMV	10	0
Syphilis (RPR+)	10	0
Toxoplasmosis	10	0
Mycoplasma	10	0

* One each of bladder, breast(2), colon, endometrial, lung, prostate, renal, and squamous(3).

II. BAL FLUID SAMPLES- Performance Characteristics

Sensitivity and specificity of the Platelia™ *Aspergillus* EIA with BAL fluid samples were evaluated in two studies in the United States on 116 samples from 62 solid organ transplant recipients and 333 samples from 116 lung transplant recipients and one study

outside the United States on 99 samples from 99 high risk hematology patients with and without invasive aspergillosis.

A. SENSITIVITY

Sensitivity was evaluated in Solid Organ Transplant and Lung Transplant recipients diagnosed with invasive aspergillosis as well as hematologic disease patients diagnosed with invasive aspergillosis according to the EORTC/MSG criteria.

I. Solid Organ Transplant recipients with Invasive Aspergillosis

Of the total of 116 samples from 62 Solid Organ Transplant recipients in one study, sensitivity was evaluated in 5 recipients diagnosed with invasive aspergillosis as shown in the table below.

Table 13

Proven or Probable Invasive Aspergillosis in Solid Organ Transplant Recipients

By Patient

Diagnosis	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Proven Aspergillosis	2	2	2/2 (100%)	34.2 - 100%
Probable Aspergillosis	3	3	3/3 (100%)	43.8 - 100%
Combined Proven and Probable Aspergillosis	5	5	5/5 (100%)	56.5 - 100%

Table 14

Proven or Probable Invasive Aspergillosis in Solid Organ Transplant Recipients By Transplant Type

Transplant Type	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Heart	1	1	1/1 (100%)	20.6 - 100%
Kidney	3	3	3/3 (100%)	43.8 - 100%
Liver	1	1	1/1 (100%)	20.6 - 100%
Total	5	5	5/5 (100%)	56.5 - 100%

II. Lung Transplant recipients with invasive aspergillosis

Of the total of 333 samples from 116 Lung Transplant recipients in another study, sensitivity was evaluated in 6 recipients diagnosed with invasive aspergillosis as shown in the table below.

Table 15

Proven or Probable Invasive Aspergillosis in Lung Transplant Recipients By patient

Diagnosis	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Proven Aspergillosis	2	1	1/2 (50.0%)	9.4 - 90.6%
Probable Aspergillosis	4	3	3/4 (75.0%)	30.0 - 95.4%
Combined Proven and Probable Aspergillosis	6	4	4/6 (66.7%)	30.0 - 90.3%

III. Hematologic disease patients with invasive aspergillosis

Sensitivity was also evaluated in a third study in 58 samples from 58 hematologic disease patients diagnosed with invasive aspergillosis as shown in the table below. In the study a retrospective analysis was performed on BAL samples from high risk hematology patients using the Platelia™ *Aspergillus* EIA. The data from this published study below was evaluated to establish the performance characteristics of the Platelia™ *Aspergillus* EIA on BAL fluid.
Maertens et al. 2009 Bronchoalveolar Lavage Fluid Galactomannan for the Diagnosis of Invasive Pulmonary Aspergillosis in Patients with Hematologic Diseases. Clin. Infec. Diseas.49:1688-93

Table 16

Proven or Probable Invasive Aspergillosis in Hematologic Disease Patients

Diagnosis	N	Index ≥ 0.5	Sensitivity	95% Confidence Interval
Proven Aspergillosis	31	31	31/31 (100%)	89.0 - 100%
Probable Aspergillosis	27	26	26/27 (96.3%)	81.7 - 99.3%
Combined Proven and Probable Aspergillosis	58	57	57/58 (98.3%)	90.8 - 99.7%

B. SPECIFICITY

Specificity was evaluated in a total of 98 BAL samples from 57 SOT recipients and 305 BAL samples from 110 Lung Transplant recipients without invasive aspergillosis and is shown in the table below. Results are presented by samples from transplant recipients with and without mold colonization.

Table 17

Specificity by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis
N = 403 BAL Fluids

Diagnosis	N	Index < 0.5	Negative (%)	95% Confidence Interval
Controls without colonization	341	330	330/341(96.8%)	94.3 - 98.2%
Controls with colonization	62	50	50/62 (80.6%)	69.1 - 88.6%
Control **Total**	403	380	380/403(94.3%)	91.6 - 96.2%

Specificity in BAL samples from the combined SOT and Lung Transplant recipients without invasive aspergillosis is presented by transplant type in the table 16 below.

Table 18

Specificity by Sample
Combined SOT and Lung Transplant Recipients without Invasive Aspergillosis
By Transplant Type
N = 403 BAL Fluids

Transplant Type	N	Index < 0.5	Negative (%)	95% Confidence Interval
Heart	28	25	25/28 (89.3%)	72.8 - 96.3%
Kidney	25	22	22/25 (88.0%)	70.0 - 95.8%
Liver	23	22	22/23 (95.7%)	79.0 - 99.2%
Lung	327	311	311/327 (95.1%)	92.2 - 97.0%
Control **Total**	403	380	380/403 (94.3%)	91.6 - 96.2%

Specificity was also evaluated in a total of 41 BAL samples from 41 hematologic disease patients without invasive aspergillosis and is shown in the table below.

Table 19

Specificity by Sample
Hemotalogic Disease Patients without Invasive Aspergillosis
N= 41

Diagnosis	N	Index < 0.5	Negative (%)	95% Confidence Interval
Control Patients	41	33	33/41 (80.5%)	66.0 – 89.8%

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

BIO-RAD Laboratories
c/o Priya Bondre
Regulatory Affairs Representative
6565 185th Ave. NE
Redmond, WA 98052

JAN 13 2011

Re: k093678

Trade/Device Name:	Platelia™ *Aspergillus* EIA
Regulation Number:	21CFR §866.3040
Regulation Name:	*Aspergillus* spp. Serological reagents.
Regulatory Class:	Class I
Product Code:	NOM
Dated:	January 7, 2011
Received:	January 11, 2011

Dear Ms. Bondre:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050. This letter will allow you to begin marketing your device as described in your Section

510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use K093678

510(k) Number (if known): Not known at this time

JAN 13 2011

Device Name: Platelia™ *Aspergillus* EIA

Indications For Use:

The Platelia™ *Aspergillus* EIA is an immunoenzymatic sandwich microplate assay for the detection of *Aspergillus* galactomannan antigen in adult and pediatric serum and Bronchoalveolar lavage (BAL) fluid samples.

The Platelia™ *Aspergillus* EIA is a test which, when used in conjunction with other diagnostic procedures such as microbiological culture, histological examination of biopsy samples and radiographic evidence, can be used as an aid in the diagnosis of invasive aspergillosis.

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K093678